Posterior Capsule Opacity Rate Superiority Claims for IOL Studies
Questions for Panel Members

Clinical Endpoints--Sugar:

- Since not all measurable PCOs are associated with clinically significant affects on a subject's visual function, do you believe that demonstration of decline in measures of visual function (eg. BCVA, glare testing, contrast sensitivity, etc.) should be a required endpoint for a PCO study? If so, what degree of visual impact (eg. >2 lines decline) do you recommend? If not, what quantitative measurement of PCO grade do you recommend as an appropriate endpoint ?

- Is a claim of delay in onset of visually significant PCO within the duration of the study clinically relevant? If so, what period of time do you consider a clinically significant delay?

- What minimum difference in PCO rate between 2 IOLs do you consider clinically significant, for which a claim of superiority should be considered? For your consideration, a sample size analysis table has been provided below for various deltas. Do you suggest a minimum number of subjects allowable for such a study?

desired Delta (difference between trial and control)	anticipated PCO rate trial IOL	anticipated PCO rate control IOL	sample size per group
10%	5%	15%	138
10%	10%	20%	157
10%	20%	30%	231
15%	10%	25%	50
15%	20%	35%	88

Study Controls--Weiss:

- What factors should be considered in choosing an appropriate control IOL? Is there a "gold-standard" control lens or PCO rate that could be designated by FDA in order to permit inter-study comparisons of PCO incidence?

- What factors are important to be matched in the trial and control populations (eg. age)?

- With regard to the HCFA NT IOL designation, what additional considerations must be factored into the choice of a control IOL for the sponsor to demonstrate superiority over all IOLs (or over a "class" of IOLs)? Do you believe it is feasible to allow claims of superiority over all IOLs with respect to PCO rate?

Methodology--Bullimore:

- Regarding current methods of PCO analysis, do you consider particular methods acceptable for PCO IOL studies? Are there particular criteria that you consider critical (eg. region of posterior capsule evaluated, level of reproducibility, etc.)? Do you consider any of the current methods not valid? Do you think that subjective clinical grading systems should be permitted (eg. comparison to standard reference photos)?

Clinical Protocol--Ferris:

- Based on review of current literature, the following exclusion criteria are proposed for PCO studies: subjects with pseudoexfoliation syndrome, uveitis, non-age-related cataracts, previous intraocular surgery or laser treatment, diabetes, glaucoma, current use of systemic steroids or topical ocular medications, previous use of cytotoxic drugs or total body irradiation, and previous ocular trauma, and intraoperative exclusions for tear in the capsulorexis, zonular dehiscence, posterior capsule rupture, vitreous loss, and other unexpected surgical complications which could reasonably be assumed to affect PCO development. Do you suggest any deletions or additions to this list?

- Regarding time points for PCO assessment, FDA guidance for IOL studies suggests scheduled follow-up at day 1, week 1, month 1, month 4-6, and years 1, 2, and 3. What time points do you suggest for PCO assessment? Do you suggest follow-up beyond 1 year? If so, at what intervals and for what duration?

- What factors are critical to be standardized within a PCO study? Across all studies? (eg. surgical techniques such as incision size, capsulorhexis size, post-op medications, and capsule polishing, as well as measurement techniques, etc.).

- If a sponsor wishes to claim reduction in Nd:YAG capsulotomy rate, what standardized clinical criteria would you suggest for performance of capsulotomy after objective documentation of PCO (ie. specified number of lines decrease and/or minimum threshold level of BCVA, contrast sensitivity, glare effect, subjective complaints, PCO grade level, or any combination of these)? Do you feel that all PCO studies should evaluate both outcomes (Nd:YAG capsulotomy rate and PCO incidence)?

Summary Question--All:

- Having reviewed the PCO study discussion paper, are there any areas for which you have additional suggestions?